

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Patent Application No. 10/576,813

Applicant: Stiefel

Filed: December 4, 2006

TC/AU: 1794

Examiner: Elizabeth A. Gwartney

Docket No.: 251508 (Client Reference No. PA35720USFZ015tel)

Customer No.: 23460

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. THOMAS STIEFEL**

1. I, Dr. Thomas Stiefel, am the inventor of the subject patent application. I currently am Managing Director of Biosyn Arzneimittel GmbH, which is the assignee of the subject patent application. A copy of my *curriculum vitae* is attached hereto as Exhibit 1.

2. In my experience, in intensive care patients, the administration of a composition comprising selenium and zinc in the ranges of 0.5-2 mg and 10-100 mg, respectively, effectively compensates for selenium deficiencies in the patient. In contrast, all other selenium supplement compositions known in the art at the time the application was filed could not adequately compensate for selenium deficiencies.

3. The following experiments were performed at my direction and under my supervision.

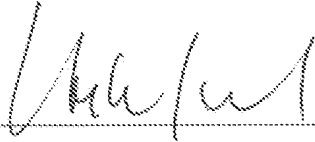
4. The efficacy of two different compositions comprising selenium and zinc were compared in intensive care patients. Specifically, a composition called Syntrace®, which comprises a daily dose of 1 mg of selenium and a daily dose of 30 mg of zinc (see Table 1 of the

present application) was compared to a composition called Tracutit®, which comprises a daily dose of 20 µg selenium, and a daily dose of 3.27 mg zinc.

5. Normal levels of selenium were achieved in the blood and serum of patients after administration of Syntrace®. In contrast, the administration of Tracutit® did not produce normal levels of selenium, either in serum or in whole blood of intensive care patients (see Exhibits 2 and 3 attached hereto).

6. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Date: 12/22/2009

  
Thomas Stiefel

## EXHIBIT 1

## EXHIBIT 1

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70184 Stuttgart  
Germany  
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### **Business and Management**

Founder and Managing Director of biosyn Arzneimittel GmbH, Germany. Founded the company in 1984 and since then through a novel approach of in-licensing, developing, standardizing and marketing of the generic compounds already in use in the field of oncology, alongside development of new and innovative biotechnology products, a business strategy of growth has been established. The company revenues have grown over the years from few thousand to millions of Euros to about 15 Million Euros in 2005. The company has grown from just 4 person in 1984 to about 90 people in 2006, which includes sales and marketing personnel for marketing of the products within Germany and other German speaking countries.

Internationalized the company in early 1990 with the establishment of offices and subsidiaries in Austria, Switzerland and USA.

Have successfully introduced the biosyn products in the world market through establishment of marketing partnership with various marketing partners in Europe, Asia and North America.

biosyn is now a recognized biotechnology company in the field of oncology especially as it relates to oncology products using hemocyanin in general and specifically keyhole limpet hemocyanin.

### **Professional and Scientific and Clinical and Quality**

Scientific and clinical development of immunotherapeutic and hemocyanin biotechnology products in oncology specifically in bladder cancer, now commercially marketed under the trade name IMMUCOTHEL®

Scientific and clinical development of selenium product(s), currently marketed under the trade name selenase® as an high dosage injection and oral form in oncology and intensive care.

Scientific and clinical development of galactose products), currently marketed under the trade name Galasyn®

Officially appointed responsible qualified person of biosyn GmbH, Germany.

Scientific research on trace elements and vitamins, amino acid and animal derived and synthetic peptide, and its application in treatment or prevention of diseases - based on which biosyn has introduced a number of products as food supplement.

Author of numerous scientific publications, patents and books

## **EXHIBIT 1**

### **Educational Qualification**

- 1968-1976** Diplomchemiker (M.Sc.) University of Stuttgart and at the Ludwig Maxmilian University, Munich, Germany. Specialization: Biochemistry
- 1976-1978** Doctorate (Ph.D.), Max Plank Institute of Metal Research, Stuttgart, Germany.  
Title of Thesis: Trace analysis of the distribution of incorporated Beryllium in whole blood and in serum proteins  
Supervisor: Professor G. Toelg

### **Experience: Name, Address and Positions held in Companies and Research Organization**

- 1978-1980** Scientist, Max Planck Institute of Metal Research, Stuttgart, Germany  
Worked on reaction and evaluation of the toxic and essential trace elements in the metabolism, specifically Be, Zn, Se and others
- 1980-1984** Head Research Department, Vitorgan Arzneimittel GmbH, Ostfildern, Germany
- 1984-Present** Managing Director, biosyn Arzneimittel GmbH, Fellbach, Germany  
Founder, managing director and officially appointed responsible qualified person of biosyn Arzneimittel GmbH, Fellbach. biosyn has the official license for GMP production of pharmaceuticals. The focus of biosyn is innovative product development and production of biotechnology product for oncology, trace elements for intensive care and oncology as well as complementary medicine in oncology. biosyn has subsidiaries in Switzerland, Austria and the United States of America.

### **Scientific Accomplishments and Professional Membership**

Originator and inventor of numerous international patents covering molecular and genetic structure, production and use of arthropod hemocyanins and arylphorins, use of selenium compounds in intensive care medicine, oncology, cardiology and composition of trace element supplements for different indications.

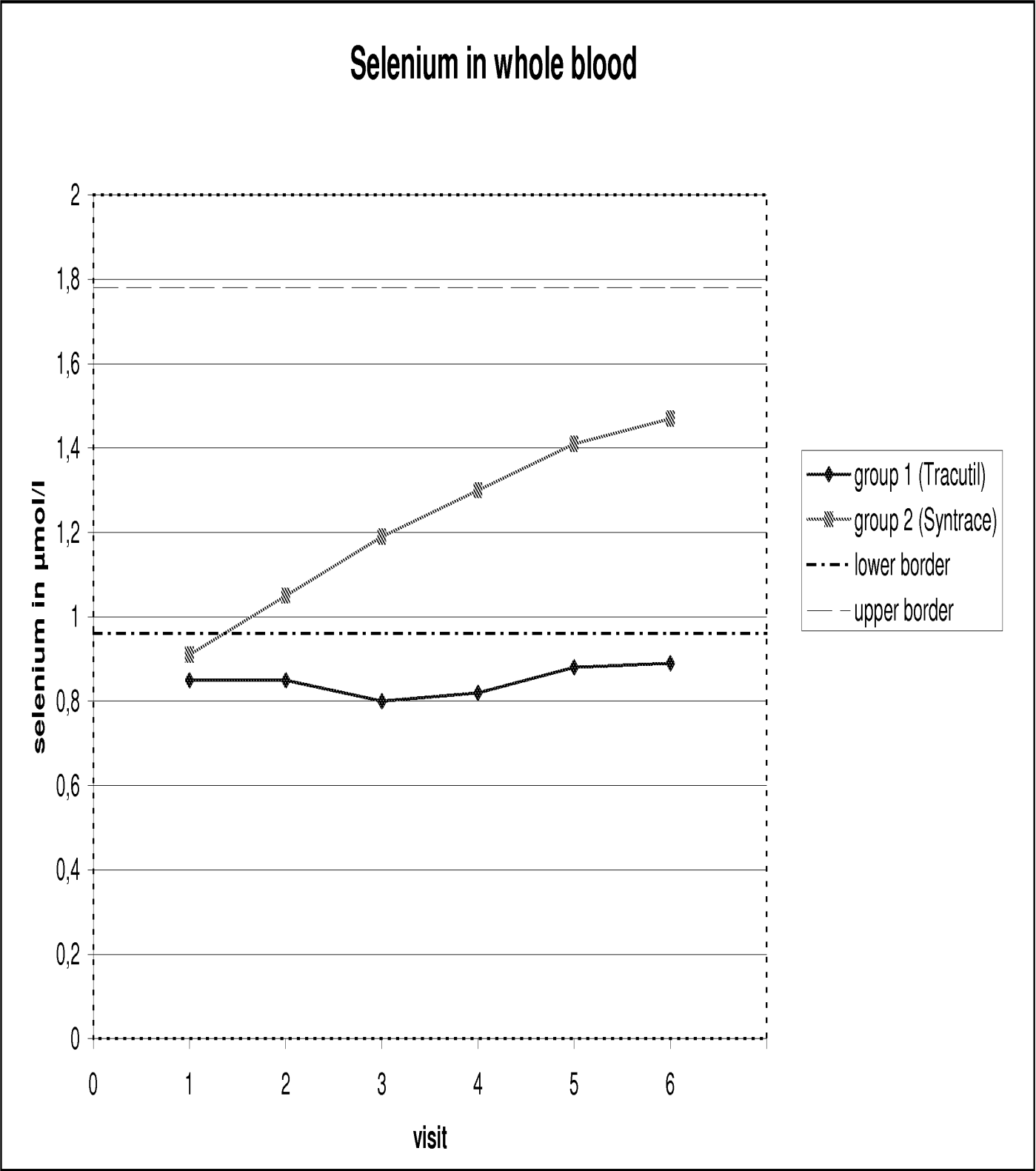
Many national and international scientific publications, including publications of symposium volumes and to several medical/scientific books.

Member Board of Directors of the Committee of Biotechnology, German Federation of the Pharmaceutical Industry (BPI).

Member - German Society of Oncology DGO, for over 20 years and he was a member of the board of directors for two years.

Member of the board of the VCI (Association of Chemical Industry) in Baden-Wuerttemberg, Germany.

## EXHIBIT 2



## EXHIBIT 3



